

A Brief Review on Fluorescent Probes for Detection of Mercury

Dilip C. Patil¹, Ravi S. Balaskar², Milind S. Thakare³, Santosh S. Dipke⁴

Assistant Professor, Department of Chemistry, Pratap College, Amalner, Dist. Jalgaon (MS), India¹

Assistant Professor, Department of Chemistry, Pratap College, Amalner, Dist. Jalgaon (MS), India²

Assistant Professor, Department of Chemistry, Pratap College, Amalner, Dist. Jalgaon (MS), India³

Assistant Professor, Department of Chemistry, Pratap College, Amalner, Dist. Jalgaon (MS), India⁴

ABSTRACT: In this review article various methods which have been used for sensing mercury, a notorious element causing serious problems to environment and human health. Present review elaborates various strategies used for sensing mercury mainly reaction based strategy, complexation and anchoring and unanchoring of fluorophores based strategies have been reported herewith.

KEYWORDS: Fluorophores, Fluoroscene, Rhodamine, Pyrene.

I. INTRODUCTION

Mercury is one of the most prevalent toxic metals in the environment and gains access to the body orally or dermally. Due to the high toxicity of mercury, considerable attention has been devoted to the development of new fluorescent chemosensors.

Recently, the study of the heavy metal cation Hg^{2+} that is known as Mercury to the general population has become ever more demanding. Most people know that mercury poisoning can happen and that it is very harmful and life threatening; however, they may not know the specific health implications involved, or what is being done to prevent Mercury poisoning. One of the ways that we can protect ourselves against the harmful effects of Mercury is by developing a chemical sensor that will be able to detect its presence in very small quantities. Numerous scientists across the globe have developed different methods in which the Mercury ion can be detected. Mercury poisoning can occur while eating fish and other marine animals. Mercury occurs naturally in the environment as the earth continues to mature and the ocean floor creates new matter. It also can be emitted into the atmosphere from everyday living habits such as fossil fuel consumption and industrial uses. When the Mercury in the environment comes into contact with bacteria it can be converted into the dangerous form of Methyl Mercury, which can cause serious health effects to humans in large enough concentrations. When the Methyl 2 Mercury is produced it can progress through the food chain starting in aquatic animals and eventually passing onto the human diet. The FDA says that most fish contain an amount of Mercury that is safe to eat. The amount of Mercury that is safe to eat is considered below the 1ppm concentration. For most small aquatic animals the concentration is almost always below this level; however, for predatory species such as shark and swordfish the concentration level may exceed 1.0 ppm, which in effect becomes hazardous to humans. People of the highest risk are those who eat fish numerous times a week. Japanese people are at considerable risk because the main source of nutrition comes from the sea and they eat aquatic life as sushi, which also increases their risk[1].

Many of the symptoms that are related to Mercury poisoning are not only serious but can also be life threatening. "There is no doubt that when humans are exposed to high levels of methyl mercury, poisoning and problems in the nervous system can occur." In the event of Mercury exposure several things may happen depending on the amount and potency of the Mercury inhaled. Mercury as an element may not cause much damage because it is a slippery and dense molecule that will be able to pass through the body; however, if the Mercury is small and absorbed through the atmosphere it can cause serious health complications. These include: Uncontrollable shake or tremor, inability to walk well, double vision, memory problems, seizures and death (only in large amounts)[2]. With the many problems that

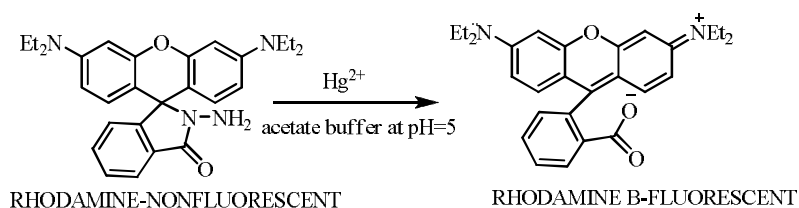
International Journal of Innovative Research in Science, Engineering and Technology

(An ISO 3297: 2007 Certified Organization)

Vol. 5, Issue 9, September 2016

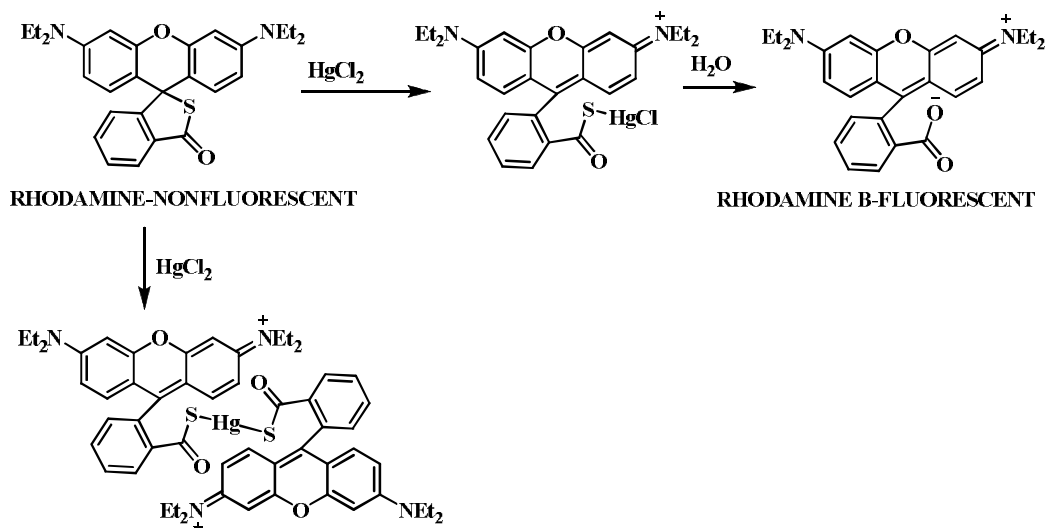
Mercury can cause it is important that society takes control of the matter and cleans up the environment to ensure that Mercury poisoning does not occur. One way in which to control this sort of contamination from happening is developing a chemical sensor that can detect the Hg^{2+} cation in very small concentrations. An ability to sense the Mercury ion enables the world to control Mercury emissions and gives the innate ability to protect us from possible danger. Therefore there has been a high demand in chemistry to develop such a sensor that can be used in industrial waste treatment and analysis of the environment. Mercury sensing has become widely popular over recent time which can be defined by its overall harmful effects to the environment and humans. Thus, there have been many scientific experiments that have been conducted to sense Hg^{2+} several of these methods will be discussed. One of these ways takes into account that Mercury can act as a reagent in chemical reaction schemes. Such a reaction involves the ring opening of a spiro lactam that when opened emits fluorescence[3]. Similar work has been done with chemodosimeters, which are mostly irreversible reactions which undergo desulfurization in the presence of Hg^{2+} . This reaction in turn changes the emission intensities[4]. While both methods mentioned are a reliable sensor for mercury they are also effected by other heavy metal ions. One question that remained to be answered is the use of the sensor in water. Alternative research used a fluorescein-based molecule which is noted for fluorescent qualities and its solubility in water. With the fluorescein base a sulfur containing group was added to make mercury more selective due to its high affinity or attraction for reaction[5]. Many challenges that are faced by these ring opening reactions include; driving the reaction towards completion, and many require excess amounts of Mercury to increase sensitivity. This problem was addressed by using a stereospecific molecule that would drive the reaction to completion. This reaction created an oxadiazole component that proved to be an effective Mercury sensor[6]. Another type of sensing that has been researched involves a large fluorescent molecule that emits different wavelengths when in contact with Mercury. This phenomena and sensor is called an excimer. When bonded to the mercury this class of molecules usually containing nitrogen and a large parent fluorescent region show ultra-violet quenching in the presence of Mercury[7].

Chang et al. [8] have explored its application in the detection of Hg^{2+} by switching the testing medium. In an acetate-buffered aqueous 10% methanol solution at pH 5, the fluorescence intensity increased rapidly upon addition of Hg^{2+} ions due to the hydrolysis of the lactam ring of the hydrazide, while an intense absorption band centered at 556 nm appeared. By monitoring the fluorescence intensity at 578 nm, the reaction between (5 μM) and 10 equiv of Hg^{2+} is complete within 10 min. The detection limit was calculated to be 0.2 μM . The fluorescence responses were observed only with the addition of Hg^{2+} , exhibiting the selectivity of toward Hg^{2+} under the present conditions.

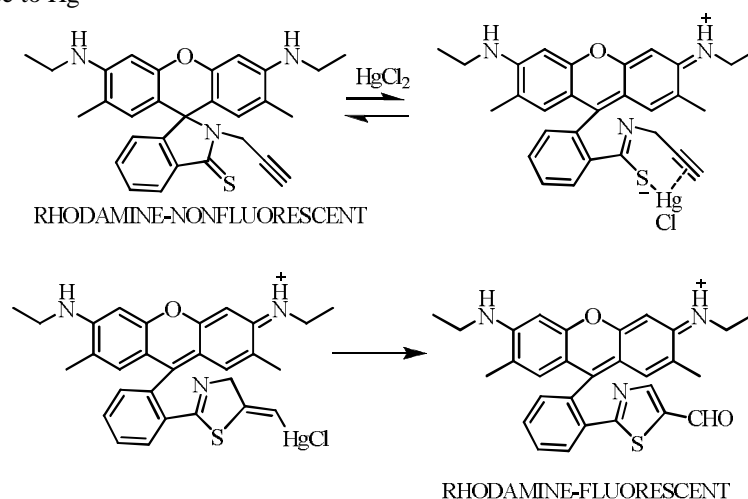


Scheme 1: Hydrolysis of 1 upon addition of Hg^{2+} in acetate buffer (pH 5)

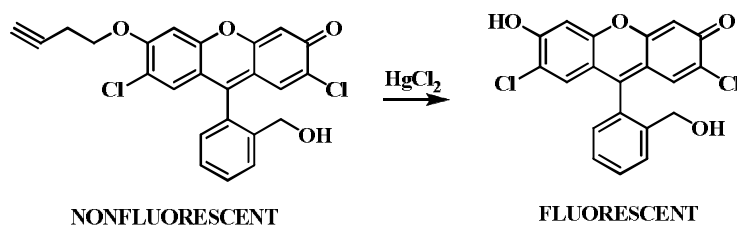
Ma et al. and Xu et al. [9,10] Independently reported the rhodamine B thiolactone as a highly selective and sensitive sensor for Hg^{2+} in 20mM phosphate buffer (pH7) and 10mM acetate buffer (pH 4). Under these conditions, displayed a selective fluorescence enhancement as well as colorimetric change only with Hg^{2+} among the various metal ions examined. Even though Xu et al. reported that this ring-opening process was reversible under their experimental conditions, Ma et al. reported that the introduction of KI to the system can reverse the color reaction only in the presence of less than 0.5 equiv of Hg^{2+} . On the basis of the ESI-MS data, Ma et al. further proposed, that complex is relatively stable in the solution; however, complex can be further degraded to rhodamine B.



Lin et al. [11] presented a rhodamine-based probe, composed of a sulfur atom and an alkyne moiety for the irreversible detection of Hg²⁺. Thiol and alkyne moieties were sited on the probe due to the thiophilic and π -philic natures of Hg²⁺. In PBS buffer (25 mM, pH 7.2, containing 20% DMF as a cosolvent), treatment with Hg²⁺ induced probe to undergo a transformation from colorless to bright yellow, as well as a dramatic enhancement (140-fold) in fluorescence. The spectral changes of probe were attributed to the formation of compounds 67-I and 67-II upon addition of Hg²⁺. A linear fluorescence response to the concentration of Hg²⁺ ranging from 5×10^{-8} to 4×10^{-6} M was observed, and the detection limit was evaluated to be 39 nM. pH effect studies imply that the probe can detect Hg²⁺ in the pH 6.0-7.4 range. Both the S atom and alkyne of probe played indispensable roles because the control compounds lacking S atoms or alkyne moieties show no response to Hg²⁺.

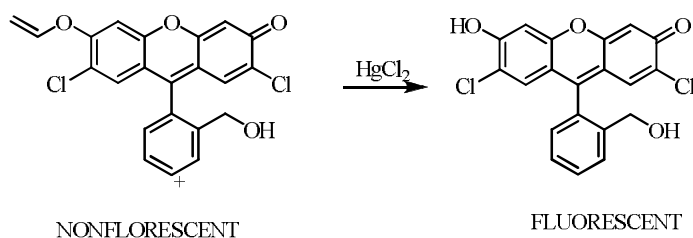


Koide and co-workers [12] used the Hg(II)-promoted hydration of alkynes, called oxymercuration, to develop a turn-on fluorescent probe for Hg(II) species. Fluorescein propargyl ether undergoes the oxymercuration to form a tautomerized keto intermediate, which further undergoes β -elimination to release the fluorescent dichlorofluorescein derivative. HgCl₂ promoted the hydration–elimination process selectively; other metal species examined showed interference less than 8%, if any. At a low concentration of the probe (0.1 mM) in pure water or in pH 7 buffer at 90 °C for 1 h, a detection limit of 8 ppb Hg²⁺ was obtained.



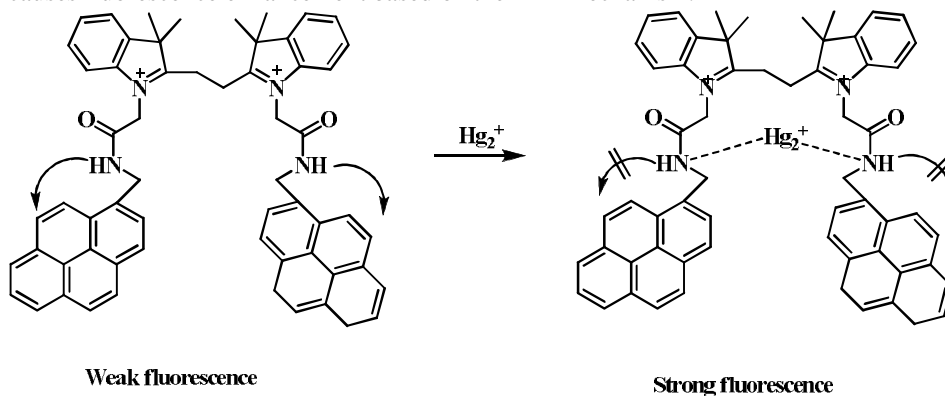
Scheme 4: Sensing of Hg(II) through oxymercuration-β-elimination of propargyl ether

Ahn and co-workers [13] developed a turn-on fluorescent probe for mercury species based on Hg (II)-promoted hydration reaction of carbon-carbon double bond (via the classical oxymercuration reaction). Fluorescein-derived vinyl ether undergoes the mercury-promoted hydration to generate the corresponding hemiacetal, which is subsequently hydrolyzed to release the highly fluorescent fluorescein derivative. Under optimized detection conditions (with 5 mM probe, in pH 7.4 PBS buffer, after 1 h at room temperature), a good linear relationship was obtained between the fluorescence increase and HgCl₂ over a wide concentration range, from which a detection limit of below 1 ppb level was obtained. A unique feature of the probe is that it is also sensitive toward methylmercury, the typical and notoriously toxic organomercury species. Other metal species exhibited only little response.



Scheme 5: Sensing of Hg (II)/methylmercury through hydrolysis of vinyl ether .

John Blecha and Haishi Cao [14] reported one fluorescent sensor using excimer mechanism to detect mercury in low concentration. In order to characterize the sensor binding to the mercury ion, was added 1 μM Hg(NO₃)₂ into a 1 μM solution of sensor . It shows fluorescence enhancement up to 30% at 405 nm . This sensor shows binding affinity to mercury ion that causes fluorescence enhancement based on the PET mechanism.



Scheme 6: The electron transfer between -NH and pyrene moiety.

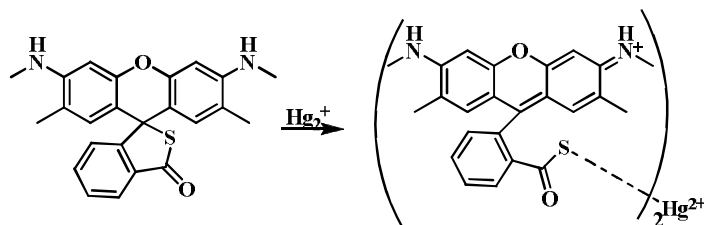
Sungsu Park, and Juyoung Yoon [15] reported rhodamine 6G thiolactone derivative which was synthesized as a selective fluorescent and colorimetric sensor for Hg²⁺ in neutral aqueous solution. “Off-on”-type fluorescent and colorimetric changes were observed only for Hg²⁺, which can be attributed to a spirothiolactone ringopening process.

International Journal of Innovative Research in Science, Engineering and Technology

(An ISO 3297: 2007 Certified Organization)

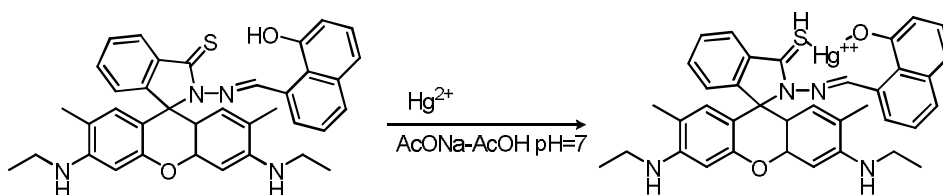
Vol. 5, Issue 9, September 2016

Since sensor can detect Hg^{2+} in the nanomolar range, this sensor has great potential for biological imaging and environmental purposes.



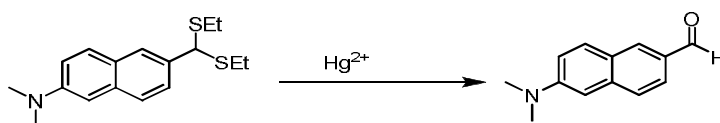
Scheme 7: spirothiolactone ringopening process initiated by Hg^{2+} .

Yinghui Wang, Yanqi Huang [16] and co-workers reported a rhodamine based cell compatible fluorescent probe for detection of Mercury. The probe was synthesized from thiohydrazide and 2-hydroxy-1-naphthaldehyde. The fluorescence spectra is recorded after gradual addition of Hg^{2+} . The probe solution Rh1 solution exhibited very weak fluorescence in the range from 510 nm to 650 nm. Upon the addition of increasing concentrations of Hg^{2+} , a new emission band peaking at 555 nm appeared and developed.



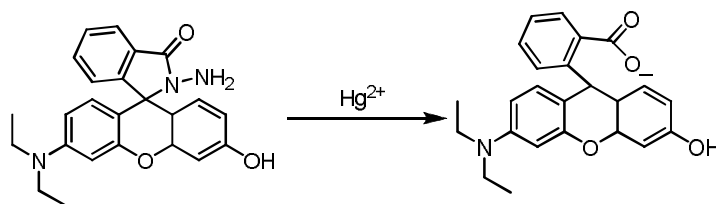
Scheme 8: Proposed binding mode of mercury with the probe

Ahn and co-workers [17] developed a reaction based strategy for detection of Hg^{2+} . The probe was prepared by the reaction of 6-formyl-2-dimethyl aminonaphthalene with ethane thiol in the presence of $\text{BF}_3 \cdot \text{Et}_2\text{O}$. The thioacetal later on exposure to Hg^{2+} undergoes desulfurization in presence of 7.4 pH buffer HEPES in presence of acetonitrile, excitation wavelength of 330 shifts to 450-550nm i.e emission wavelength



Scheme 9: reaction based strategy for detection of mercury.

Yan-Ru Zhang,^a Qing-Rong Wang [18] and co-workers developed a selective probe Rhodol hydrazide for detection of mercury ions, the probe can be used in green solvents like water and ethanol. The probe has high selectivity for mercury ions. The absorbance and fluorescence study shows linear relationship with concentration of mercury $^{2+}$



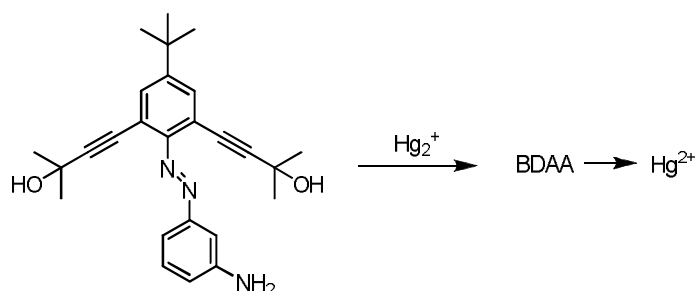
Scheme 10: reaction based strategy for detection of Hg^{2+} .

International Journal of Innovative Research in Science, Engineering and Technology

(An ISO 3297: 2007 Certified Organization)

Vol. 5, Issue 9, September 2016

Yuliang Li and co-workers [19] came up with an off/on fluorescence sensor for detection of mercury ions in aqueous media. The probe was prepared by diazotization of 2,6-bis(3-methyl-3-hydroxy-1-butynyl)-4-tert-butyl aniline which later diazocoupled with-dianiline to yield respective probe. Fluoremetric study was performed in HEPES buffer at biological pH 7.4.



Scheme 10: Complexation based strategy for detection of Hg²⁺.

REFERENCES

- [1] Young-Seoub Hong, Yu-Mi Kim, and Kyung-Eun Lee, "Methylmercury Exposure and Health Effects", *J Prev Med Public Health*. 45(6) (2012): 353–363.
- [2] Foulke, Judith. "Mercury in Fish: Cause for Concern" U. S. Food and Drug Administration, FDA Consumer, September 1994; Revised May 1995.
- [3] Lee, M. H.; Wu, J.; Lee, J.; and Jung, J. H.; Kim, J. S., "Highly sensitive and selective chemosensor for Hg²⁺ based on the rhodamine fluorophore", *Org. Lett.* 9 (2007): 2501-2504.
- [4] Liu, B.; and Tian, H., "A selective fluorescent ratiometric chemodosimeter for mercury ion" *Chem. Comm.* 25 (2005): 3156-3158
- [5] Nolan, E., and Lippard, S. J., "A 'Turn-On' Fluorescent Sensor for the Selective Detection of Mercuric Ion in Aqueous Media", *J. Am. Chem. Soc.* 125(47) (2003): 14270-14271
- [6] Yang, Y. K., Yook, K. J., and Tae J., "A rhodamine-based fluorescent and colorimetric chemodosimeter for the rapid detection of Hg²⁺ ions in aqueous media", *J. Am. Chem. Soc.* 127(48) 2005, 16760-16761
- [7] Yasuhiro, Y., Maehara, H., Ishizumi, K., and Hirai, T., "A Rhodamine-Cyclen Conjugate as a Highly Sensitive and Selective Fluorescent Chemosensor for Hg(II)", *Org. Lett.* 73(21) (2007): 3125-3128.
- [8] Kim, K. N.; Choi, M. G.; Noh, J. H.; Ahn, S.; Chang, S.-K., "Ratiometric Signaling of Hg²⁺ Ions by a Fluorescein-Coumarin Chemodosimeter" *Bull. Korean Chem. Soc.* 31(1) (2008): 246-249.
- [9] Shi, W.; Ma, H., "Rhodamine B thiolactone: a simple chemosensor for Hg²⁺ in aqueous media" *Chem. Commun.* 16 (2008), 1856-1858.
- [10] Zhan, X.-Q.; Qian, Z.-H.; Zheng, H.; Su, B.-Y.; Lan, Z.; Xu, J.-G., "Rhodamine thiospirolactone. Highly selective and sensitive reversible sensing of Hg(II)", *Chem. Commun.* 16 (2008): 1859-1861.
- [11] Lin, W.; Cao, X.; Ding, Y.; Yuan, L.; Long, L., "A highly selective and sensitive fluorescent probe for Hg(2+) imaging in live cells based on a rhodamine-thioamide-alkyne scaffold" *Chem. Commun.* 46(20) (2010): 3529-3531.
- [12] Lin, W.; Cao, X.; Ding, Y.; Yuan, L.; Yu, Q., "A reversible fluorescent Hg²⁺ chemosensor based on a receptor composed of a thiol atom and an alkene moiety for living cell fluorescence imaging" *Org. Biomol. Chem.* 8(16) (2010): 3618-3620.
- [13] M. Santra, S.-K. Ko, I. Shin and K. H. Ahn., "Fluorescent detection of palladium species with an O-propargylated fluorescein" *Chem. Commun.*, 46 (2010): 3964-3966.
- [14] John Blecha and Haishi Cao. "highly selective pyrene based fluorescent sensor toward Hg²⁺ detection", *Tetrahedron Letters* 51(26) (2010): 3422-3425.
- [15] Xiaoqiang Chen, Seong-Won Nam, Min Jung Jou, Youngmee Kim, Sung-Jin Kim, Sungsu Park, and Juyoung Yoon, "Hg²⁺ selective fluorescent and colorimetric sensor: its crystal structure and application to bioimaging" *Org. Lett.* 10(22) 2008: 5235-5238.
- [16] Yinghui Wang, Yanqi Huang, Bin Li, Liming Zhang, Hang Song, Hong Jianga and Jie Gao, "A cell compatible fluorescent chemosensor for Hg²⁺ based on a novel rhodamine derivative that works as a molecular keypad lock", *RSC Adv.*, 1 (2011): 1294–1300.
- [17] Alla Sreenivasa Rao, Dokyoung Kim, Taejun Wang, Ki Hean Kim, Sekyu Hwang, and Kyo Han Ahn., "Reaction-Based Two-Photon Probes for Mercury Ions: Fluorescence Imaging with Dual Optical Windows.", *Org. Lett.*, 14(10) 2012: 2598–2601
- [18] Yan-Ru Zhang, Qing-Rong Wang, Peng Su, Fei Zhao, Jun Huang and Bao-Xiang Zhao., "A simple yet effective fluorescent probe for detecting and imaging mercury ions in cells" *RSC Adv.*, 5 (2015): 20634-20638.
- [19] Maozhong Tian, Libing Liu, Yongjun Li, Ruifeng Hu, Taifeng Liu, Huibiao Liu, Shu Wang, Yuliang Li, "An Unusual OFF-ON Fluorescence Sensor for Detecting Mercury Ions in Aqueous Media and Living Cell", *Chem. Commun.*, 50 (2014): 2055-2057.